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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,453	09/26/2006	Michael Kretschmar	LNK-019	1342

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,453	KRETSCHMAR ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 1-18 are pending and currently under examination.

Priority: This application claims foreign priority to German application 102004044429.3, filed September 14, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a precipitate of a plasma fraction to form at a pH between 4.7 and 5.3, does not reasonably provide enablement for a precipitate to form at any pH below 5.4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The scope of the instant claims is not commensurate with the enablement of the instant disclosure, because practice of the claimed invention would require undue experimentation by an artisan of ordinary skill in the art to ascertain which pH values below 5.4 will cause the plasma fraction to form a precipitate. Therefore, there could be many pH values to choose from. Thus for the instant claimed invention, it would require an undue burden of experimentation for a skilled artisan to determine exactly which pH values below 5.4 will cause the plasma fraction to form a precipitate.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case the quantity of experimentation would be large since there are many pH values below 5.4 to choose from. The amount of guidance in the specification is zero with regard to which pH values below 5.4, besides the preferred range of pH 4.7 to 5.3, will allow a precipitate to form that is commensurate with the instant invention. The examples in the specification support a pH value between 4.7 and 5.3. The nature of the invention is such that a deviation and/or change outside the preferred pH range may or may not cause a precipitate to form that is commensurate with the instant invention. The state of the prior art is that methods of separating and purifying a protein are highly sensitive to their physical environments. The

relative level of skill in this art is very high. The predictability as to a precipitate forming is zero.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claim is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn to a process for separating fibronectin from a plasma fraction comprising the steps of (i) and (ii). However, it is not clear how fibronectin is being separated in the steps as currently recited in (i) and (ii). Further clarification is requested.

Similarly, claim 2 is drawn to a process for the production of a composition containing a coagulation factor comprising the steps of (i) and (ii). It is not clear how a composition containing a coagulation factor is produced according to the steps of (i) and (ii). Further clarification is requested.

Claim 7 recites the limitation "the fibronectin precipitate" in the claim. There is insufficient antecedent basis for this limitation in the claim and its parent claim.

Claim 9 recites the limitation "the concentration of NaCl or KCl" in the claim. There is insufficient antecedent basis for this limitation in the claim and its parent claim.

Claim 15 recites solvent/detergent treatment. It is unclear which solvent is intended or if "solvent" is a "detergent solvent". Further clarification is requested.

Claims 3-6, 8, 10-14, 16-18 are included in this rejection because they are dependent on the above claims and fail to cure the defect.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, 10-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Zykova et al. (1983 Voprosy Meditsinskoi Khimii 25(5): 114-117 abstract; IDS). Zykova et al. teach a method for the precipitation of fibronectin at pH 5.0 (abstract; claims 1, 3-5, 10-11).

Claims 1-5, 6, 8, 10-11, 14, 16, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Wallace et al. (US 4341764). Wallace et al. teach a method for preparing fibronectin and antihemophilic factor from blood plasma comprising the steps of: forming a solution of blood plasma fraction in an aqueous medium, acidifying the solution to a pH sufficient to form an acid precipitate, separating the acid-precipitate from the solution, isolating fibronectin from the precipitate, and isolating antihemophilic factor from the solution (col. 9-10 lines 1-21; claims 1-5, 10-11, 16, 18). Wallace et al. further teach that the solution can be acidified at a pH of about 5.0 to form the acid precipitate (col. 9 line 13; claims 1-5, 10-11).

Wallace et al. also teach the plasma fraction is dissolved cryoprecipitate (col. 9 line 9, col. 5 line 28; claim 14). In Example 1, Wallace et al. teach the acid precipitate contains 260 g protein (col. 5 line 34; claim 8). After precipitation, the precipitate suspension was stirred for 3 hours (col. 5 lines 50-53; claim 6).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764). The teachings of Wallace et al. are outlined above. Wallace discloses the acid-precipitate was separated by centrifugation. Wallace et al. do not teach separation by means of an agitator blade of a stirrer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that the separation of the acid-precipitate from the plasma fraction can be done by any acceptable means known in the art, i.e. the blade of a stirrer, since techniques for separating a precipitate from a solution are routine in the art (claim 7).

Claims 9, 12-13, 15, 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burnouf-Radosevich et al. (US 5408039) in view of Winkelman (US 4789733). Burnouf-

Radosevich et al. disclose a process for purifying human von Willebrand factor (vWF) from a cryoprecipitated plasma fraction, which comprises a series of purification steps (col. 5-7). Burnouf-Radosevich et al. disclose aluminum hydroxide treatment to remove fibronectin (col. 5 lines 43-49), a solvent-detergent treatment to destroy lipid enveloped viruses (col. 5 lines 57-60), and an anion exchange chromatographic step (col. 6). After the anion exchange chromatographic step, Burnouf-Radosevich et al. disclose that the vWF eluate reveals a slight contamination by fibronectin (col. 6 lines 66-68). Burnouf-Radosevich et al. do not teach to precipitate fibronectin by lowering the pH.

Winkelman discloses the purification of a blood coagulation factor (VIII) by precipitation. Winkelman discloses blood plasma fraction pH can be adjusted such that as pH decreases to 6.0, the precipitation of fibronectin increases.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate a vWF protein from a cryoprecipitated plasma fraction comprising the purification steps of Burnouf-Radosevich and coupled with the fibronectin precipitation step of Winkelman (claims 9, 15, 17). One of ordinary skill would be motivated to adjust the pH to less than 6.0, i.e. pH 5.0, because it would be reasonable to assume that a pH lower than 6.0 will further increase the precipitation of fibronectin. Further, one of ordinary skill would recognize that plasma naturally contains the components of natural salts, i.e. NaCl or KCl, and amino acids, i.e. glycine (claims 12-13).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

January 30, 2008